BAUSCH Health

Relistor® (Methylnaltrexone Bromide) Data is Published in the Journal of Emergency Medicine

December 22, 2021

Data from a Post-Hoc Analysis Supports the Use of Salix's RELISTOR for Patients with Opioid-Induced Constipation and Advanced Illness in the Emergency Department Setting

LAVAL, QC, Dec. 22, 2021 /PRNewswire/ -- Bausch Health Companies Inc. (NYSE/TSX: BHC) "Bausch Health" and its gastroenterology business, Salix Pharmaceuticals ("Salix"), one of the largest specialty pharmaceutical companies in the world committed to the prevention and treatment of gastrointestinal diseases, today announced that *The Journal of Emergency Medicine* has published a new post-hoc analysis of pooled results on the safety and efficacy of a single dose of RELISTOR® (methylnaltrexone bromide) injection in patients with severe illness and opioid-induced constipation (OIC) who had insufficient response to laxative therapy.

Entitled, "*First Dose Efficacy of Methylnaltrexone in Patients with Severe Medical Illness and Opioid-Induced Constipation: A Pooled Analysis*," the study results demonstrated that an initial dose of RELISTOR injection effectively produced rescue-free laxation (RFL) in greater proportions of severely ill patients with OIC compared to placebo (61.4% within 4 hours vs. 16%, and 72.1% within 24 hours vs. 40.1%).

OIC is prevalent among patients with advanced illness presenting to the emergency department (ED). In particular, patients who are prescribed opioids for advanced illness who experience constipation have a significantly increased risk of emergency department visits, hospitalization rates, treatment costs and medical costs. The objective of this post hoc analysis of pooled results from three randomized, placebo-controlled trials was to assess the efficacy and safety of a single RELISTOR injection dose for OIC patients with severe medical illness, having insufficient response to laxative therapy and impairment of functional status.

"In this analysis, the rapid onset of RELISTOR demonstrates how it provides early rescue-free laxation without compromising opioid analgesia," said Dr. Frank Peacock, lead author and director of research at Baylor College of Medicine. "The publication of this data set supports the value of RELISTOR as being clinically useful for the types of patients who frequently visit the emergency department for OIC."

Per the study, there was no observable effect of RELISTOR injection treatment on the efficacy of opioid analgesia, indicating that pain control was maintained. Side effects of RELISTOR were mostly gastrointestinal in nature, including abdominal pain, flatulence, nausea, and vomiting, and declined from treatment day one to day two.

About RELISTOR

RELISTOR® (methylnaltrexone bromide) is an opioid antagonist. RELISTOR tablets and RELISTOR injection are indicated for the treatment of opioid-induced constipation (OIC) in adults with

chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

RELISTOR injection is also indicated for the treatment of OIC in adults with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care.

RELISTOR is not indicated to reduce all-cause mortality for opioid-induced bowel disorders.

IMPORTANT SAFETY INFORMATION

- RELISTOR tablets and injection are contraindicated in patients with known or suspected mechanical gastrointestinal obstruction and patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation.
- Cases of gastrointestinal perforation have been reported in adult patients with opioid-induced constipation and advanced illness with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the gastrointestinal tract (e.g., peptic ulcer disease, Ogilvie's syndrome, diverticular disease, infiltrative gastrointestinal tract malignancies or peritoneal metastases). Take into account the overall risk-benefit profile when using RELISTOR in patients with these conditions or other conditions which might result in impaired integrity of the gastrointestinal tract wall (e.g., Crohn's disease). Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue RELISTOR in patients who develop this symptom.
- If severe or persistent diarrhea occurs during treatment, advise patients to discontinue therapy with RELISTOR and consult their health care provider.
- Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, and yawning have occurred in patients treated with RELISTOR. Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal and/or reduced analgesia and should be monitored for adequacy of analgesia and symptoms of opioid withdrawal.
- Avoid concomitant use of RELISTOR with other opioid antagonists because of the potential for additive effects of opioid receptor antagonism and increased risk of opioid withdrawal.
- The use of RELISTOR during pregnancy may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because of the potential for serious adverse reactions, including opioid withdrawal, in breastfed infants, advise women that breastfeeding is not recommended during treatment with RELISTOR. In nursing mothers, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.
- A dosage reduction of RELISTOR tablets and RELISTOR injection is recommended in patients with moderate and severe renal impairment (creatinine clearance less than 60 mL/minute as estimated by Cockcroft-Gault). No dosage adjustment of RELISTOR tablets or RELISTOR injection is needed in patients with mild renal impairment.
- A dosage reduction of RELISTOR tablets is recommended in patients with moderate (Child-Pugh Class B) or severe (Child- Pugh Class C) hepatic impairment. No dosage adjustment of RELISTOR tablets is needed in patients with mild hepatic impairment (Child-Pugh Class A). No dosage adjustment of RELISTOR injection is needed for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, monitor for methylnaltrexone-related adverse reactions and dose adjust per Prescribing Information as may be indicated.
- In the clinical studies, the most common adverse reactions were:

  <u>OIC in adult patients with chronic non-cancer pain</u>

  - RELISTOR tablets (≥ 2% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (14%), diarrhea (5%), headache (4%), abdominal distention (4%), vomiting (3%), hyperhidrosis (3%), anxiety (2%), muscle spasms (2%), rhinorrhea (2%), and chills (2%).
  - RELISTOR injection (≥ 1% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (21%), nausea (9%), diarrhea (6%), hyperhidrosis (6%), hot flush (3%), tremor (1%), and chills (1%).
- <u>OIC in adult patients with advanced illness</u>
  - RELISTOR injection (≥ 5% of RELISTOR patients and at a greater incidence than placebo): abdominal pain (29%) flatulence (13%), nausea (12%), dizziness (7%), and diarrhea (6%).

To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800- FDA-1088 or
www.fda.gov/medwatch

Please click
here
for full Prescribing Information for RELISTOR tablets and RELISTOR injection.

About Salix
Salix Pharmaceuticals is one of the largest specialty pharmaceutical companies in the world committed to the prevention and treatment of gastrointestinal diseases. For more than 30 years, Salix has licensed, developed and marketed innovative products to improve patients' lives and arm health care providers with life-changing solutions for many chronic and debilitating conditions. Salix currently markets its product line to U.S. health care providers through an expanded sales force that focuses on gastroenterology, hepatology, pain specialists and primary care. Salix is headquartered in Bridgewater, New Jersey. For more information about Salix, visit
www.Salix.com
and connect with us on
Twitter
and
LinkedIn
.

About Bausch Health
Bausch Health Companies Inc. (NYSE/TSX: BHC) is a global company whose mission is to improve people's lives with our health care products. We develop, manufacture and market a range of pharmaceutical, medical device and over-the-counter products, primarily in the therapeutic areas of eye health, gastroenterology and dermatology. We are delivering on our commitments as we build an innovative company dedicated to advancing global health. For more information, visit
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Forward-looking Statements
This news release may contain forward-looking statements, which may generally be identified by the use of the words "anticipates," "hopes," "expects," "intends," "plans," "should," "could," "would," "may," "believes," "estimates," "potential," "target," or "continue" and variations or similar expressions. These statements are based upon the current expectations and beliefs of management and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include, but are not limited to, the risks and uncertainties discussed in the Bausch Health most recent annual report on Form 10-K and detailed from time to time in Bausch Health's other filings with the U.S. Securities and Exchange Commission and the Canadian Securities Administrators, which factors are incorporated herein by reference. They also include, but are not limited to, risks and uncertainties caused by or relating to the evolving COVID-19 pandemic, and the fear of that pandemic and its potential effects, the severity, duration, and future impact of which are highly uncertain and cannot be predicted, and which may have a material adverse impact on Bausch Health, including but not limited to its project development timelines, and costs (which may increase). Readers are cautioned not to place undue reliance on any of these forward-looking statements. These forward-looking statements speak only as of the date hereof. Bausch Health undertakes no obligation to update any of these forward-looking statements to

reflect events or circumstances after the date of this news release or to reflect actual outcomes, unless required by law.

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